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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,733	06/12/2000	CHARLES ZUKER	02307E-085110US	6739

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/463,733	ZUKER, CHARLES	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-13,15,17,19,20,22,24 and 28-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-13,15,17,19,20,22,24 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on December 12, 2005 has been entered.

Claims 1, 5-13, 15, 17, 19, 20, 22, 24, and 28-31 are pending. All previous grounds of rejection are withdrawn in view of Applicant's amendments to the claims. However, the following new grounds of rejection now apply to the claims. This action is made non-final.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-13, 15, 17, 19, 20, 22, 24, and 28-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The specification as originally filed does not appear to provide basis for the amendment to the claims to recite a method of screening for modulators of RDGC GPCR phosphatase activity wherein the method includes providing a second sample containing a mutant rhodopsin lacking the last 18 amino acids at the cytoplasmic terminus, exposing the second sample to a test compound, detecting RDGC GPCR phosphatase activity in the second sample and comparing the level of RDGC GPCR phosphatase activity of the second sample with a first sample.

In the response filed December 12, 2005, Applicants point to original claims 14, 23 and 32 and to page 44 of the specification as providing support for this amendment.

However, original claims 14, 23 and 32, refer to methods of screening for modulators of RDGC GPCR phosphatase activity wherein the assays include providing a second sample containing a **mutant RDGC phosphatase**. These claims do not provide support for the concept of performing the screening assay using a **mutant rhodopsin**.

The specification at page 44 does disclose a mutant rhodopsin protein in which the COOH-terminal 18 amino acids have been deleted (i.e., Rh1Δ356). The specification (pages 43-44) also teaches an assay in which "RDGC was analyzed biochemically, physiologically, and genetically to determine its activity as a GPCR phosphatase." In these assays, transgenic flies expressing the truncated rhodopsin were analyzed, as were flies expressing wildtype rhodopsin. The specification reports

that "(t)he truncated receptor was expressed in near normal amounts and the cells displayed normal light response. Rhodopsin was not hyperphosphorylated in Rh1Δ356 flies."

However, the specification does not disclose the use of the truncated rhodopsin mutant in methods of screening for modulators of RDGC phosphatase activity wherein phosphatase activity is compared in samples containing wildtype rhodopsin and samples containing the truncated rhodopsin. Regarding in vitro and in vivo assays for modulators of RDGC phosphatase, the specification (e.g., page 22) teaches that the results obtained with rhodopsin and a test compound are compared to "control samples or animals without the test compound." There is no disclosure of using a control sample which contains the test compound and truncated rhodopsin. Accordingly, the specification as originally filed does not appear to set forth the concept of comparing the results obtained with samples containing wildtype rhodopsin to samples containing mutant rhodopsin lacking the last 18 amino acids at the cytoplasmic terminus, to thereby identify modulators of RDGC GPCR phosphatase activity.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-13, 15, 17, 19, 20, 22, 24, and 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5-13, 15, 17, 19, 20, 22, 24, and 28-31 are indefinite because the claims do not recite a clear nexus between the preamble of the claims and the final

process step of the claims. The claims are drawn to methods of screening for modulators of RDGC GPCR phosphatase activity. However, the final step of the methods is one which thereby detects RDGC GPCR phosphatase activity. Accordingly, it is unclear as to whether the claims are intended to be limited to methods which screen for modulators of RDGC GPCR phosphatase activity or methods which detect RDGC GPCR phosphatase activity. This rejection may be overcome by amendment of the claims to recite at step (vi) "thereby detecting modulators of RDGC GPCR phosphatase activity."

Claims 1 and 5-13 are indefinite because the phrase in step (vi) of "the first sample" lacks proper antecedent basis.

Claims 15, 17, 19, 20 and 22 are indefinite because the phrase in step (vi) of "the first sample" lacks proper antecedent basis. While the claims previously refer to a "cell sample," the claims do not previously refer to a "first sample."

Claims 24 and 28-31 are indefinite over the recitations in step (vi) of "the first sample" because this phrase lacks proper antecedent basis. The claims previously refer to an animal, but do not previously refer to first sample. Also, since the method is one which occurs in vivo, it is unclear as to whether "the second sample" is considered to be an animal or some other type of sample. Additionally, in claim 24, step (iii) "a second sample comprising" should be amended to refer to the step of providing a second sample/animal.

4. Claims 1, 5-13, 15, 17, 19, 20, 22, 24, and 28-31 are allowable over the prior art for the following reasons:

The closest prior art of Byk teaches a method comprising providing a first sample of eye membranes containing wild-type RDGC and a second sample of eye membranes containing mutant RDGC; contacting the sample with a compound (such as calcium or arrestin) which is suspected of having the ability to modulate RDGC GPCR phosphatase activity, and detecting RDGC GPCR phosphatase activity by means of a phosphorylation assay that is conducted by measuring mobility on an electrophoretic gel (see figures 2 and 5, and page 1909). Byk teaches that the GPCR rhodopsin is a major substrate for RDGC phosphatase (page 1908) and specifically exemplifies methods which monitor calcium and arrestin for their ability to modulate dephosphorylation of rhodopsin by RDGC.

Zuker teaches a method of measuring membrane potential changes in intact *Drosophila* photoreceptor cells and calcium changes in *Drosophila* transgenic for rhodopsin (Figure 4). Zuker (page 575) further states that "It is here where the study of phototransduction in *Drosophila* offers unprecedented versatility. The study of this signal cascade in the fruit fly *Drosophila melanogaster* makes it possible to use powerful molecular genetic techniques to identify novel transduction molecules and then to examine the function of these molecules *in vivo*, in their normal cellular and organismal environment". Furthermore, Zuker (GenBank Accession No. M17718) teaches the isolated nucleic acid sequence of *Drosophila* RDGC, wherein the sequence is identical to present SEQ ID NO: 1.

Chen (Science. 1995. 267: 374-377; cited in the IDS) teaches that rhodopsin is inactivated by phosphorylation near the carboxyl terminus (see abstract). Chen teaches

mutants of rhodopsin wherein the carboxy terminal 15 amino acids have been deleted (see Figure 1). The reference reports that "removal of 15 amino acids from the COOH-terminus of rhodopsin produces a molecule that is transported to the rod outer segment and activates transducin normally but fails to be shut off properly. Phosphorylation of rhodopsin at the COOH-terminus is presumably essential for rapid termination of the photoresponse in vivo" (page 377). Chen does not teach or suggest rhodopsin mutants having a deletion of the last 18 amino acids at the COOH-terminus, as is required by the present claims. Further, Chen does not teach the effect of deleting the COOH-terminal 18 amino acids on the functional activity of rhodopsin, particularly with respect to the dephosphorylation of rhodopsin by RDGC phosphatase.

Weiss (Biochemistry. 1994. 33: 7587-7593) teaches rhodopsin mutants in which the COOH-terminal 24 amino acids have been deleted (i.e., the K325stop mutant; see abstract and Figure 1). With regard to the GTPγS-binding assay and G_t activation, Weiss reports that the K325stop mutants were approximately 30% more active than wildtype rhodopsin (page 7591). Weiss does not teach or suggest rhodopsin mutants having a deletion of the last 18 amino acids at the COOH-terminus. Further, Weiss does not teach the effect of deleting the COOH-terminal 18 amino acids on the functional activity of rhodopsin, particularly with respect to the dephosphorylation of rhodopsin by RDGC phosphatase.

In summary, the claims are allowable over the prior art because the prior art does not teach or suggest methods of screening for modulators of RDGC phosphatase activity wherein the methods comprise exposing a first and second sample to a test

compound and to RDGC phosphatase comprising the sequence of SEQ ID NO: 1, wherein the first sample comprises rhodopsin and the second sample comprises a mutant rhodopsin lacking the last 18 amino acids at the cytoplasmic terminus and comparing the level of RDGC phopshatase activity in the first and second sample to thereby identify a compound that modulates RDGC phosphatase activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
February 1, 2006

CARLA J. MYERS
PRIMARY EXAMINER